

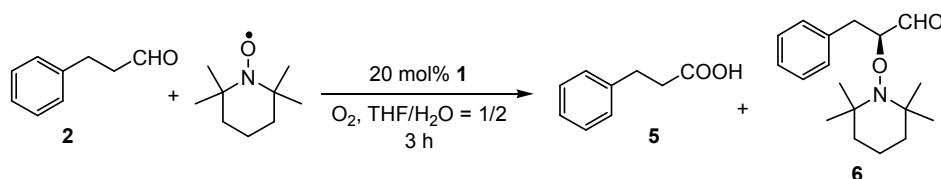
One-pot sequential alcohol oxidations and asymmetric α -oxyamination in aqueous media using recyclable resin-supported peptide catalyst

*Kengo Akagawa, Takuma Fujiwara, Seiji Sakamoto, Kazuaki Kudo**

General information.

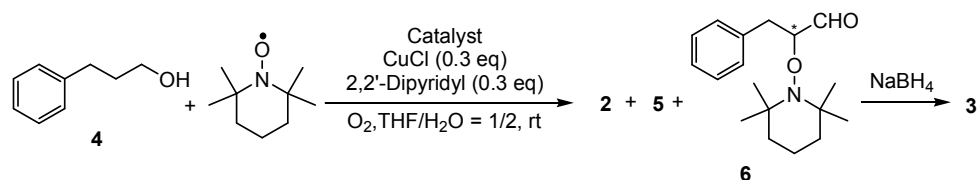
^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively on a JEOL JNM-LA400 spectrometer, and chemical shifts were referenced to internal tetramethylsilane (TMS, $\delta = 0.0$ ppm) for ^1H , the central line of CDCl_3 ($\delta = 77.0$ ppm) for ^{13}C . PEG-PS supported peptide catalyst **1** was synthesized according to the same method as previously described.^{8,9c} HPLC analyses were carried out on a Shimadzu CLASS-VP system using Chiralcel OD-H column (25 cm) and OD-H guard (1 cm), Chiralpak IA column (25 cm) and IA guard (1 cm), or Chiralcel OJ (25 cm). FAB mass measurements were performed on JEOL JMS-600H.

Examinations of reaction conditions for α -oxyamination of aldehyde: To estimate the reaction efficiency in α -oxyamination of an aldehyde with copper(I) chloride, the ratio of starting aldehyde **2**, carboxylic acid **5**, and desired product **6** was analyzed by ^1H NMR measurement of crude mixtures.

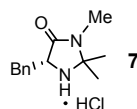


Entry	Conditions	2 : 5 : 6
1	TEMPO (2 eq), CuCl (0.3 eq), 0 °C	5 : 73 : 22
2	TEMPO (4 eq), CuCl (0.1 eq), rt	14 : 40 : 46
3	TEMPO (4 eq), CuCl (0.3 eq), rt	0 : 32 : 68

Optimization of reaction conditions for tandem reaction starting from alcohol: The ratio of starting alcohol **4**, aldehyde **2**, carboxylic acid **5**, and desired product **6** was analyzed by ^1H NMR measurement of crude mixtures.

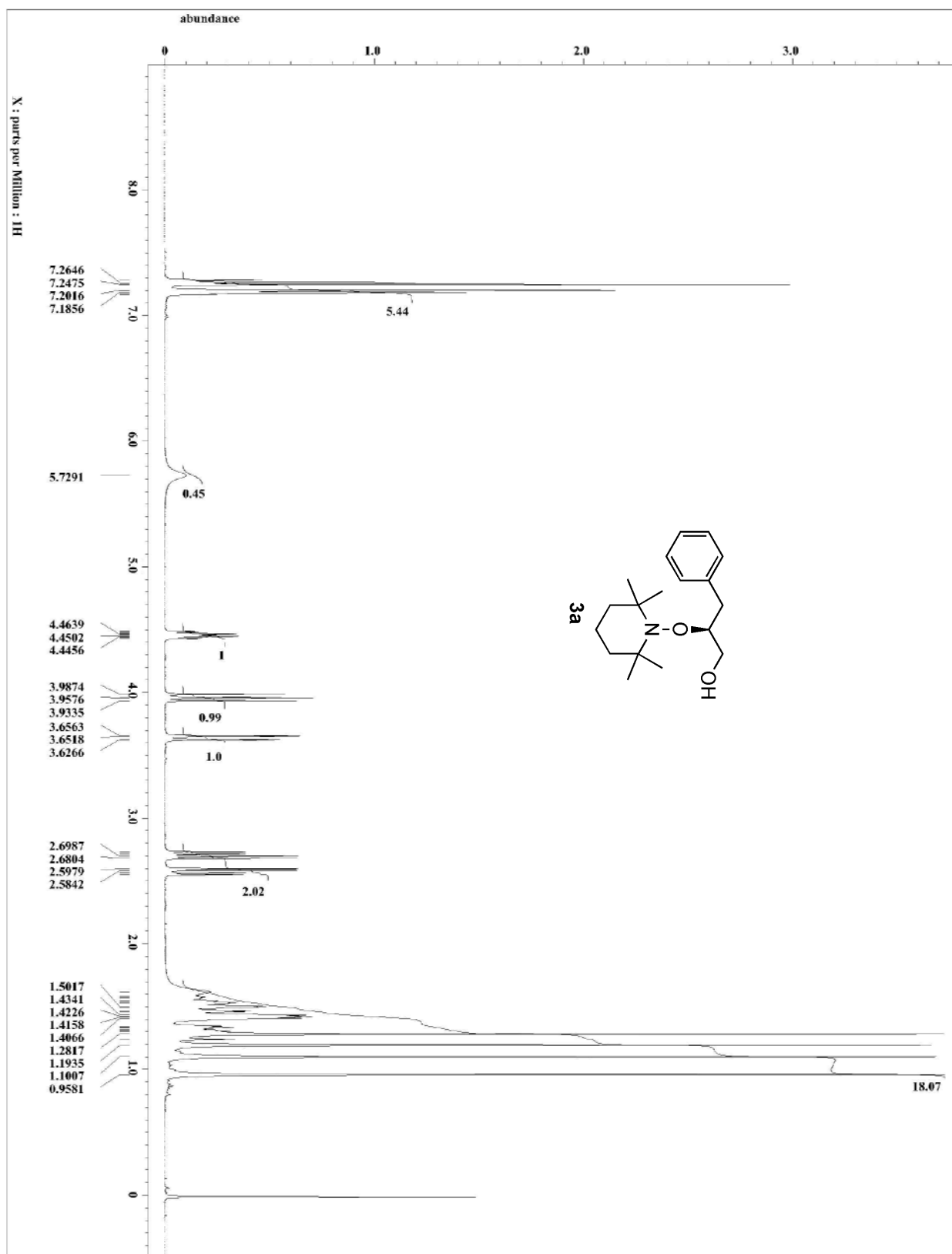


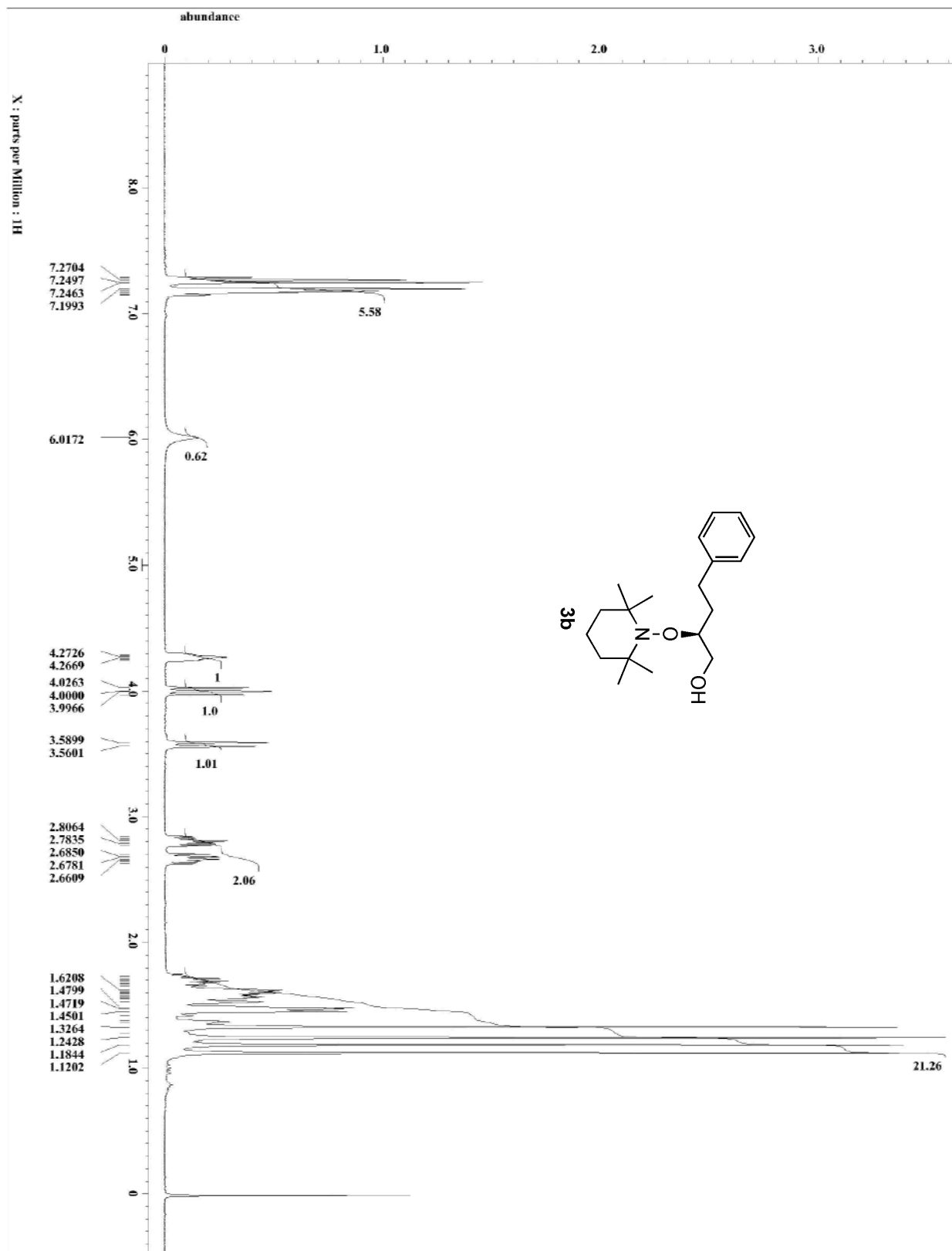
Entry	Catalyst	TEMPO	Concentration of 4	Time	4 : 2 : 5 : 6	3
1	1 (0.05 eq)	2 eq	0.4 M	24 h	23 : 6 : 50 : 21	13% yield, 89% ee [<i>S</i>]
2	1 (0.2 eq)	4 eq	0.2 M	24 h	5 : 0 : 22 : 73	57% yield, 90% ee [<i>S</i>]
3	1 (0.2 eq)	4 eq	0.1 M	24 h	12 : 0 : 12 : 76	62% yield, 93% ee [<i>S</i>]
4	1 (0.2 eq)	4 eq	0.1 M	36 h	not determined	66% yield, 93% ee [<i>S</i>]
5	7 (0.2 eq)	4 eq	0.1 M	36 h	31 : 7 : 34 : 28	28% yield, 66% ee [<i>R</i>]

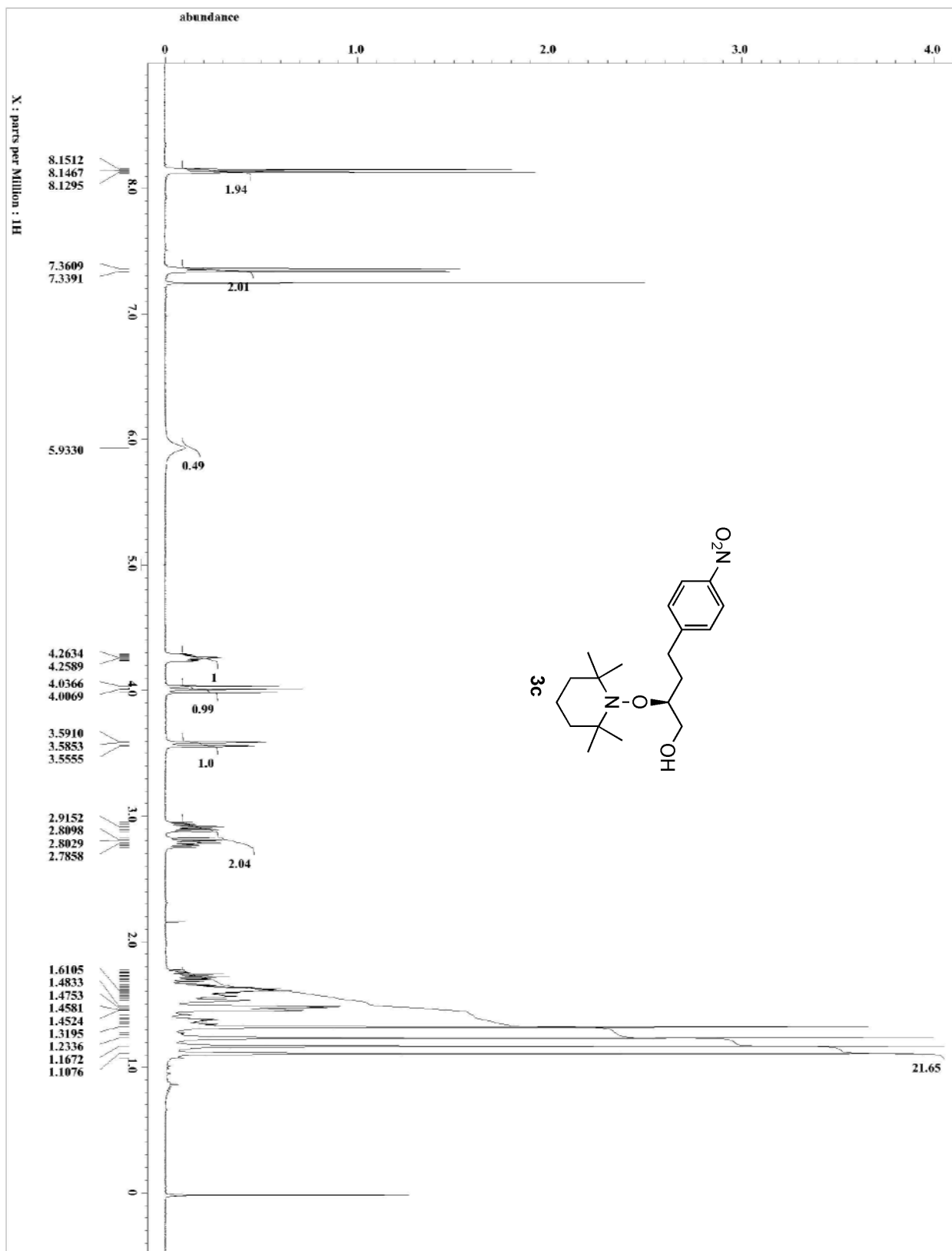


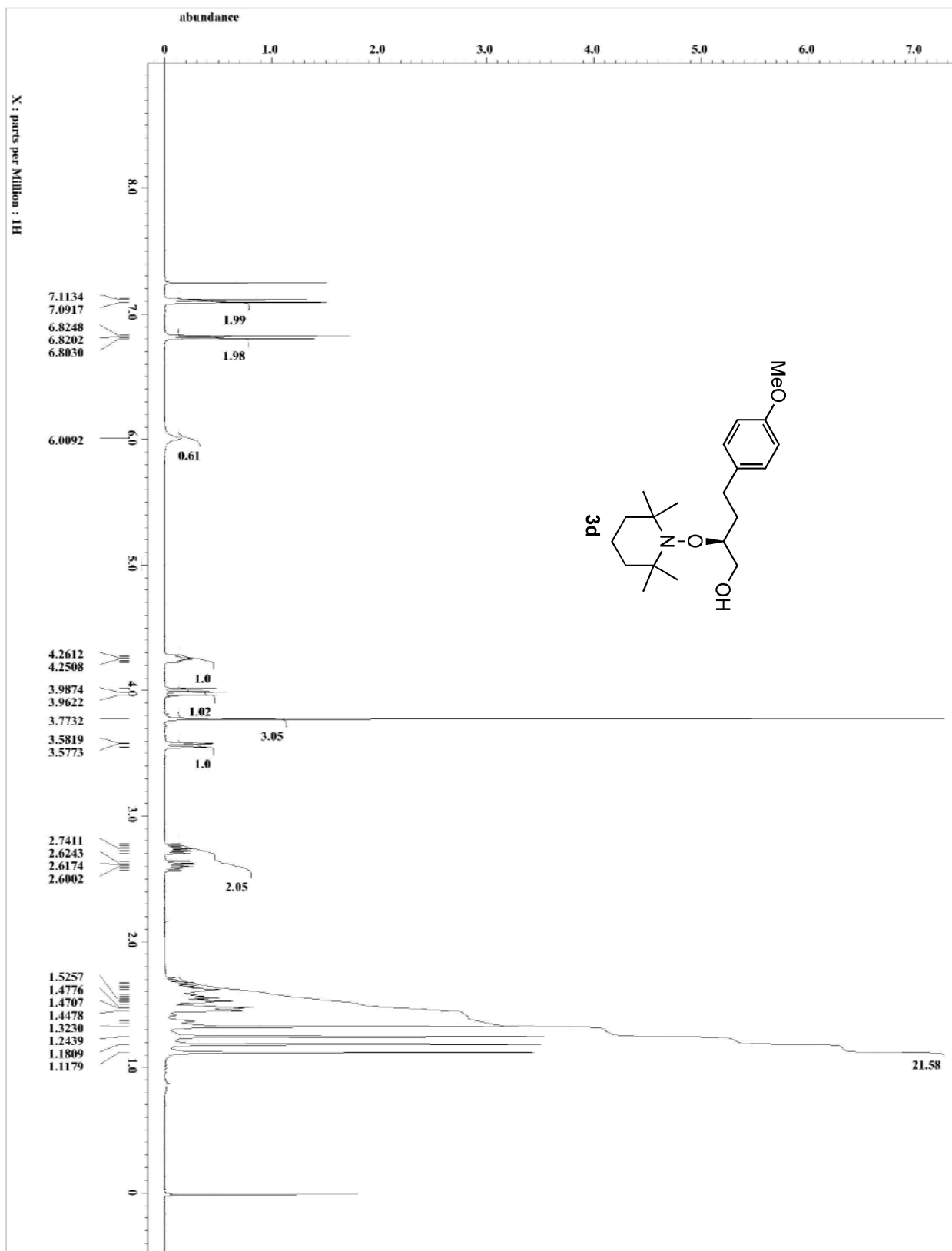
All products obtained in Table 2 are known compounds. Enantiomeric excesses and the absolute configurations of products **3a-f** were determined according to the literature.⁶

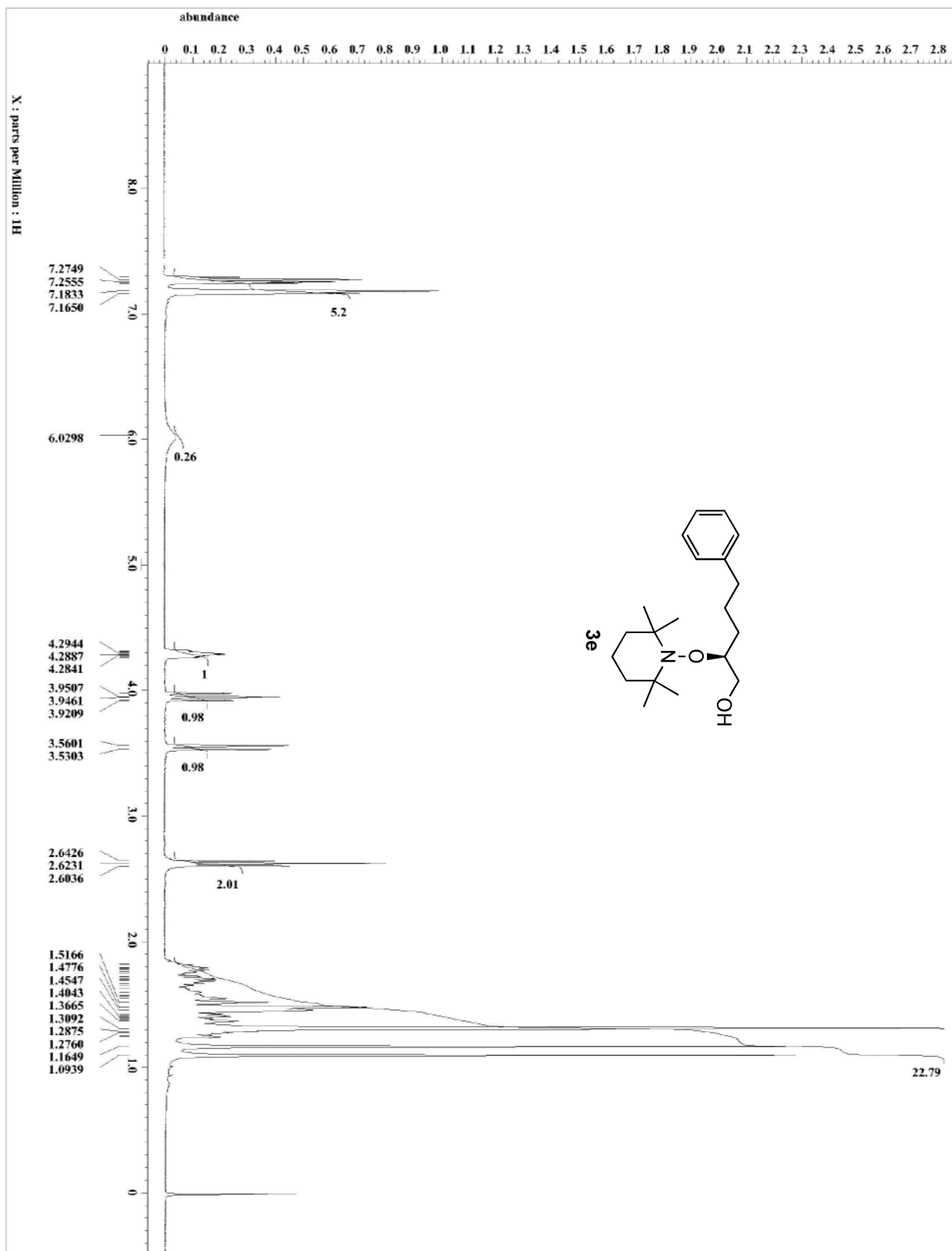
^1H NMR spectra

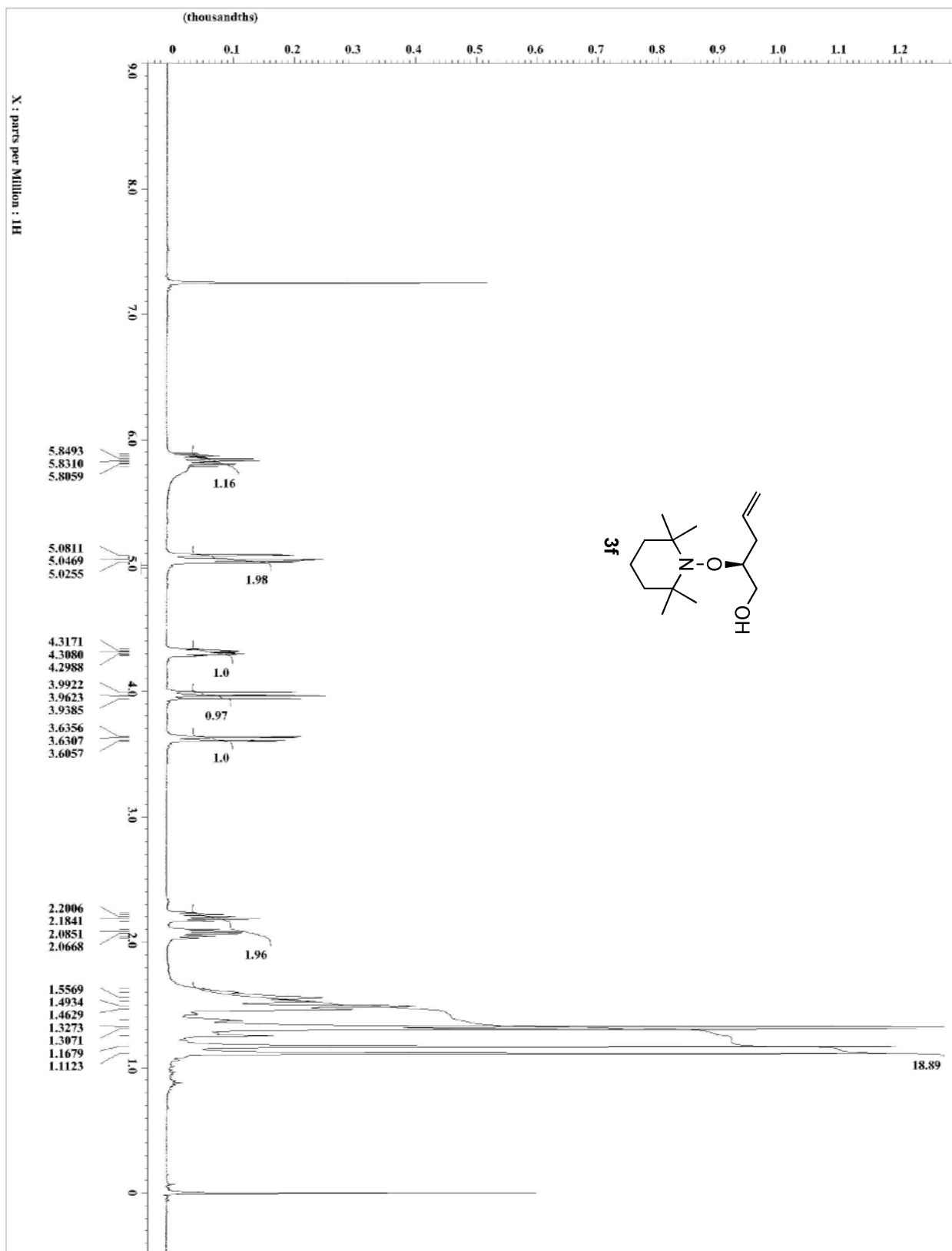


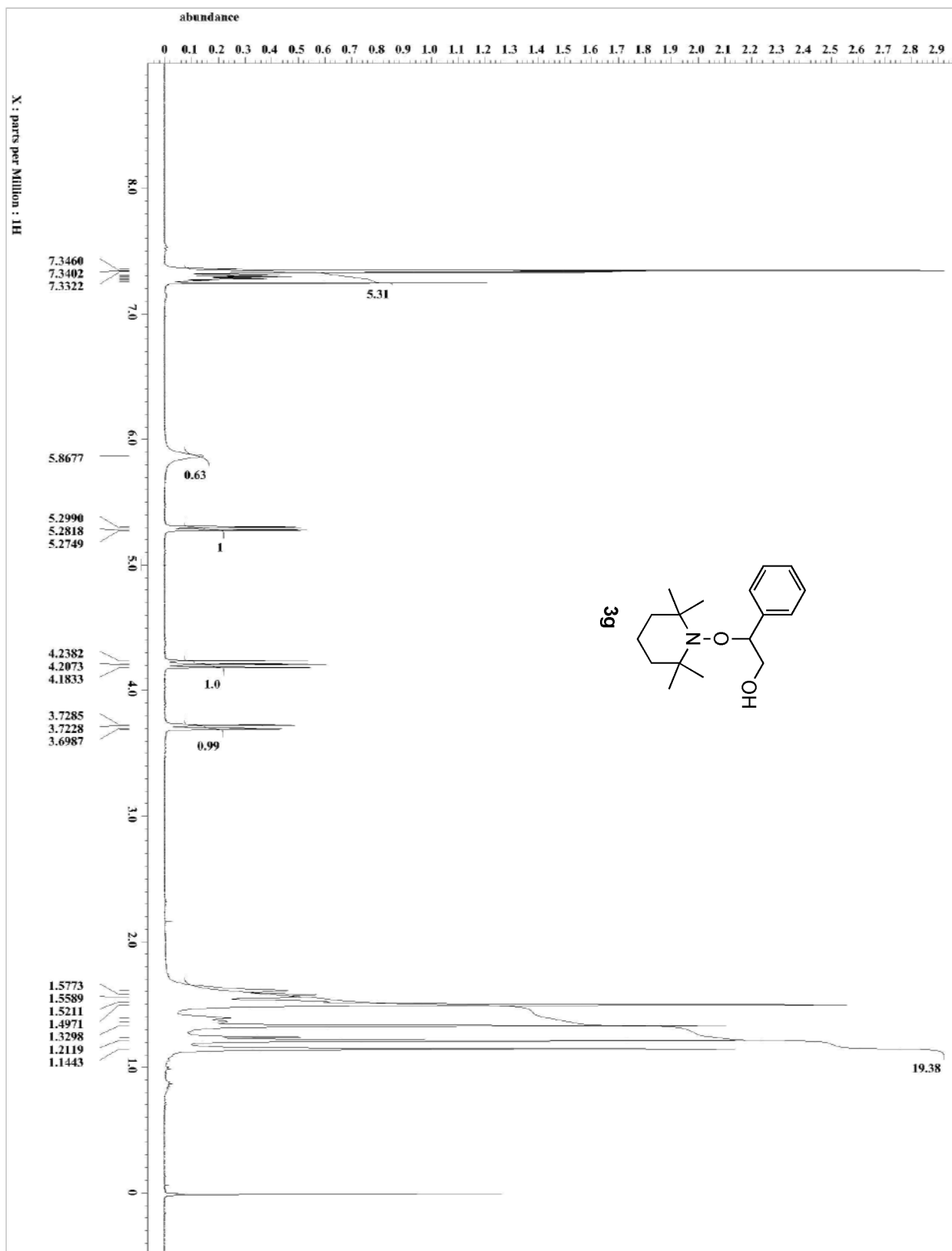




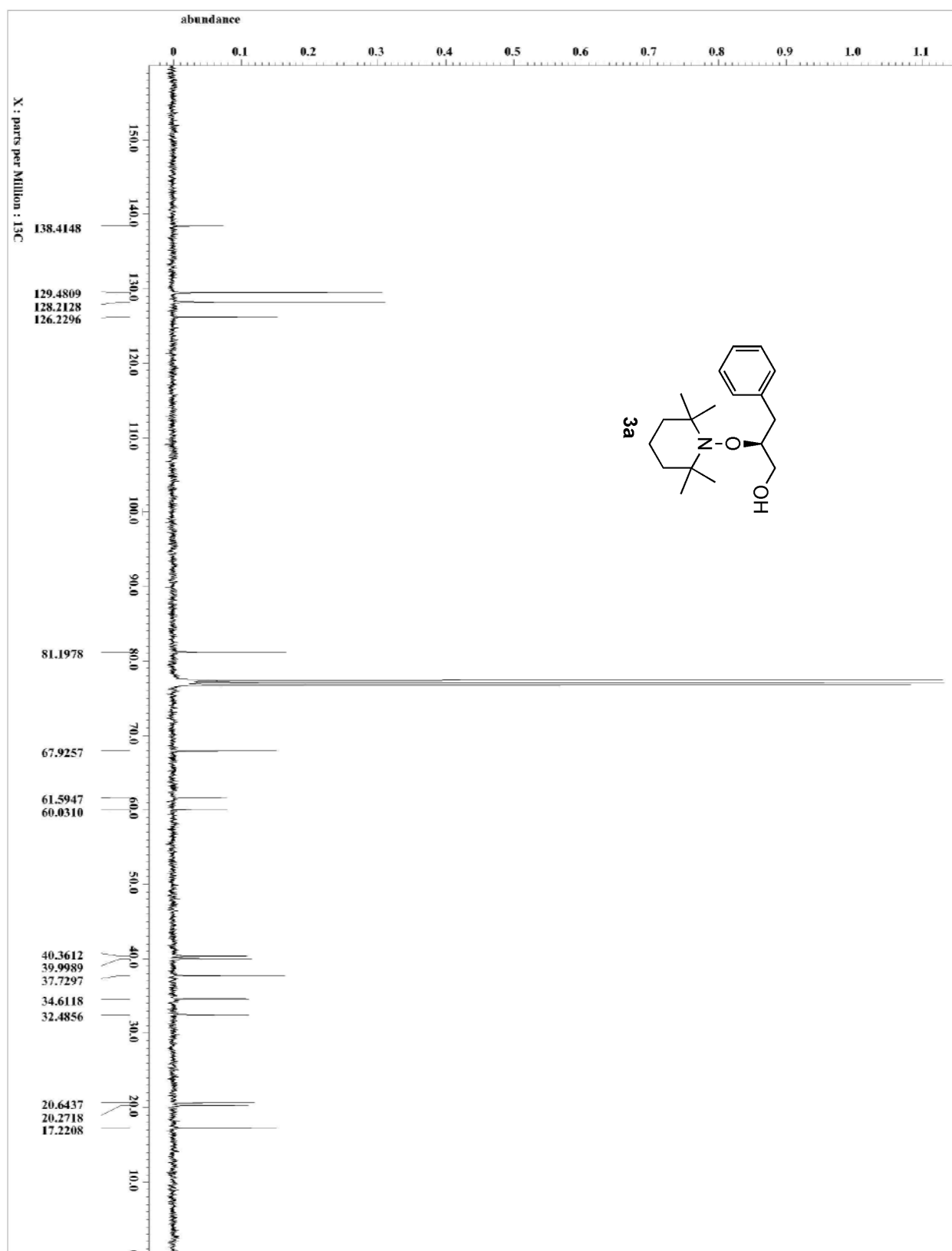


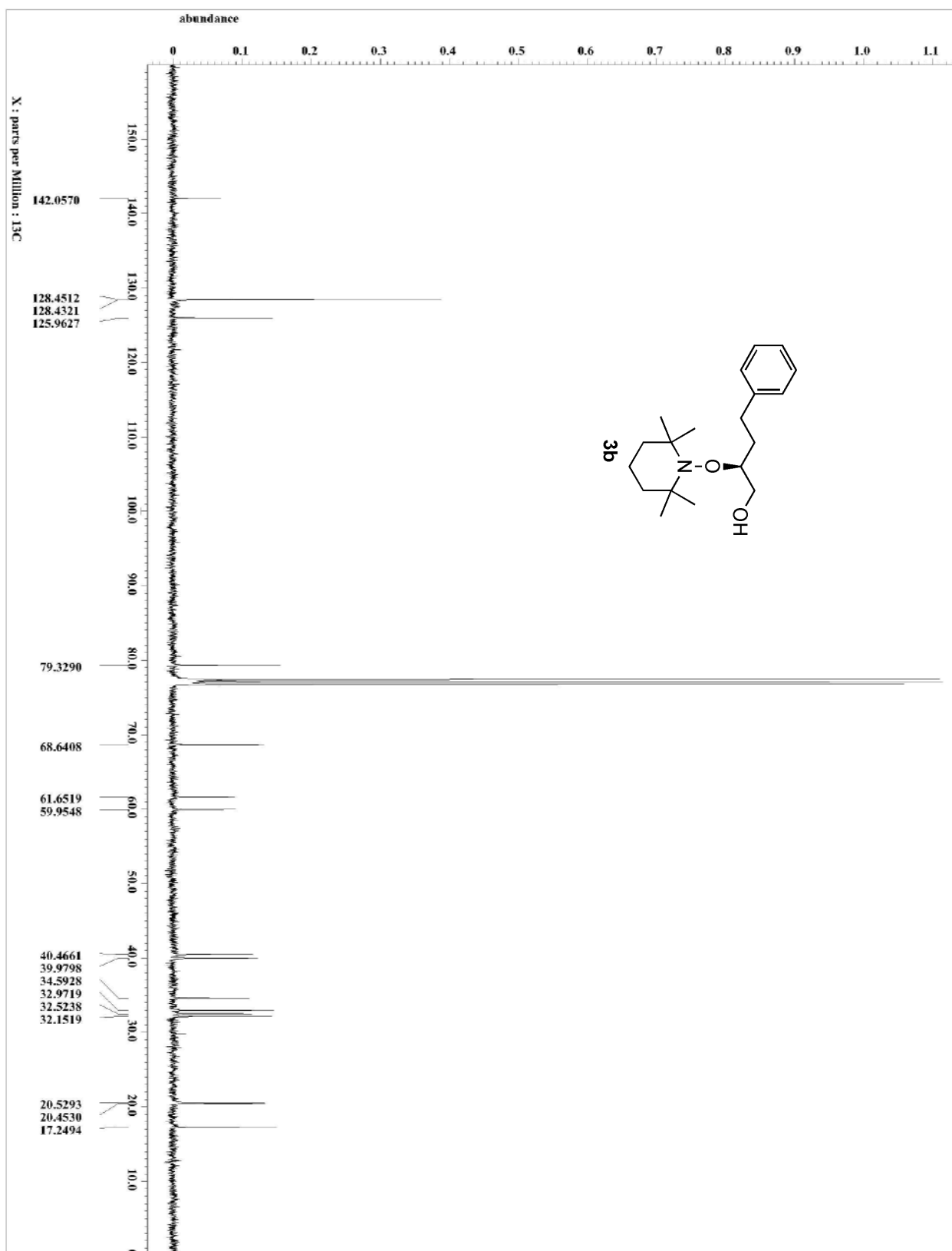


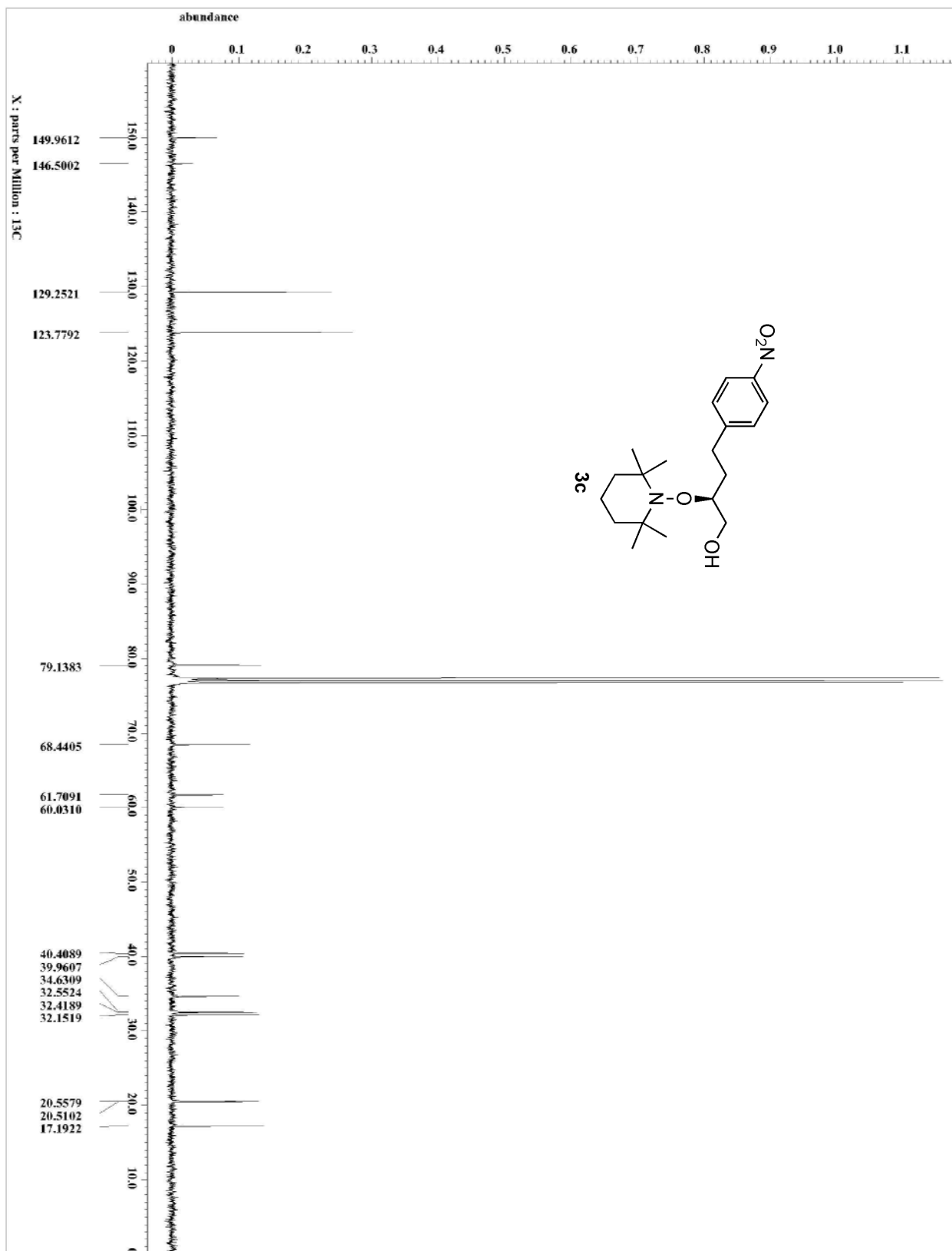


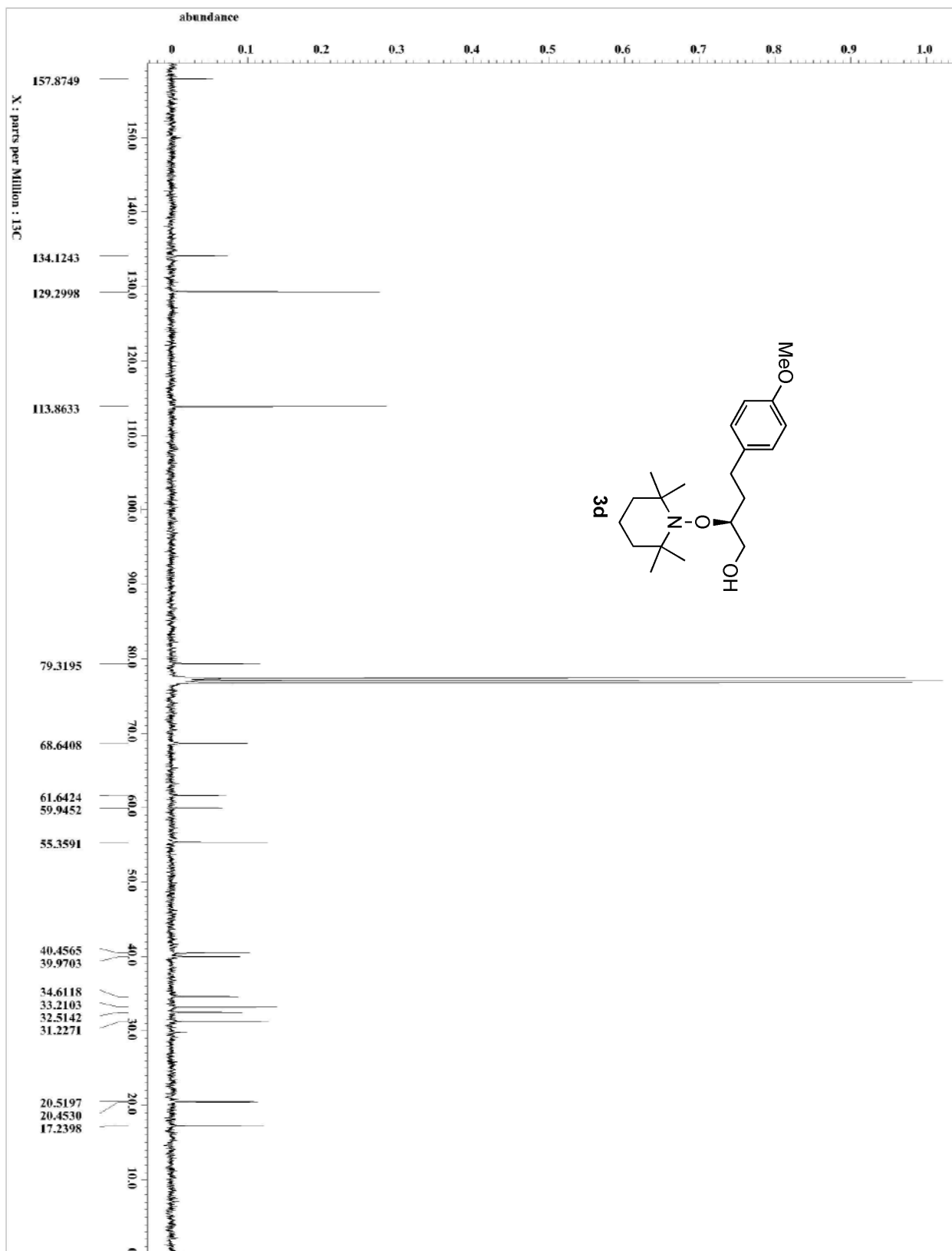


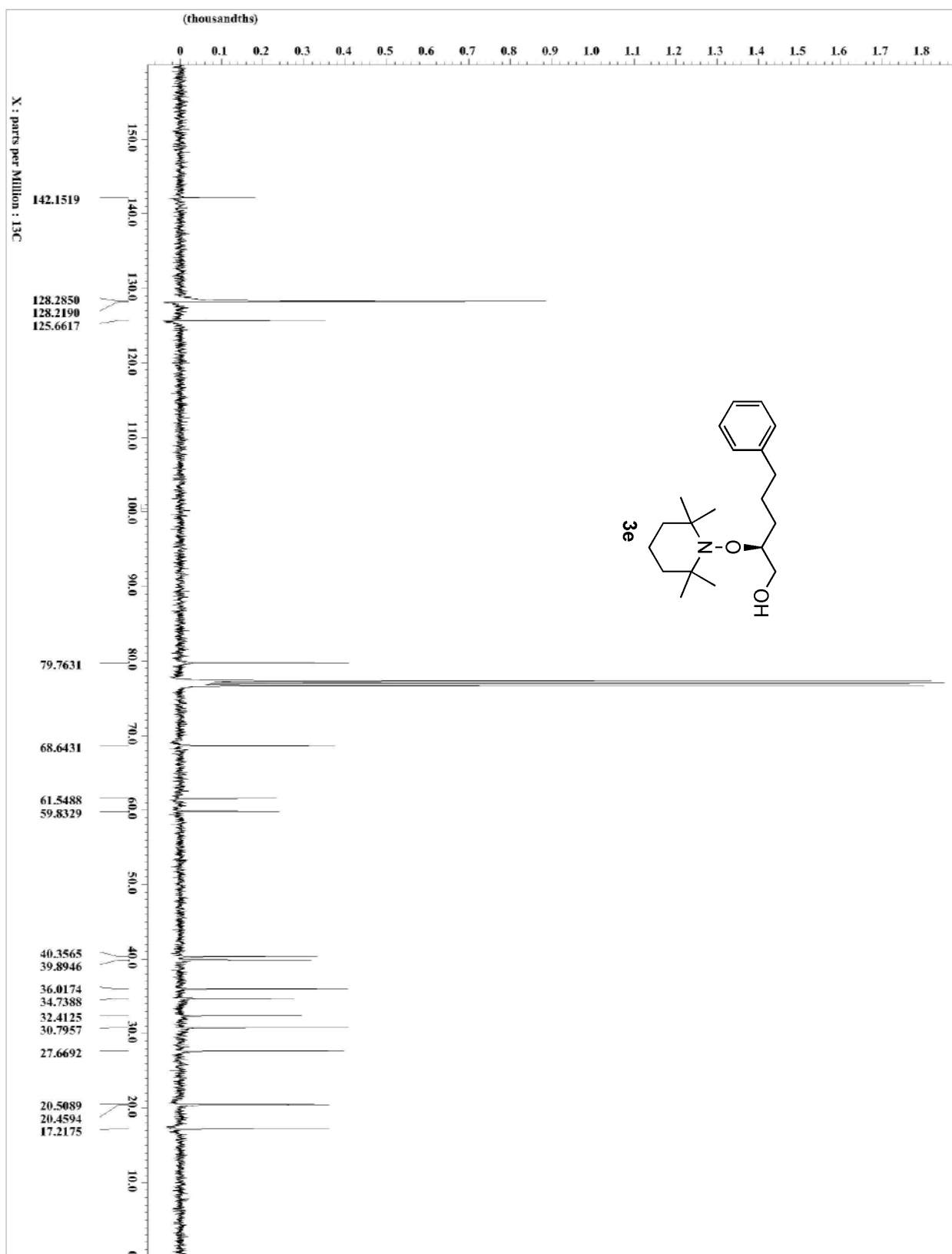
^{13}C NMR spectra

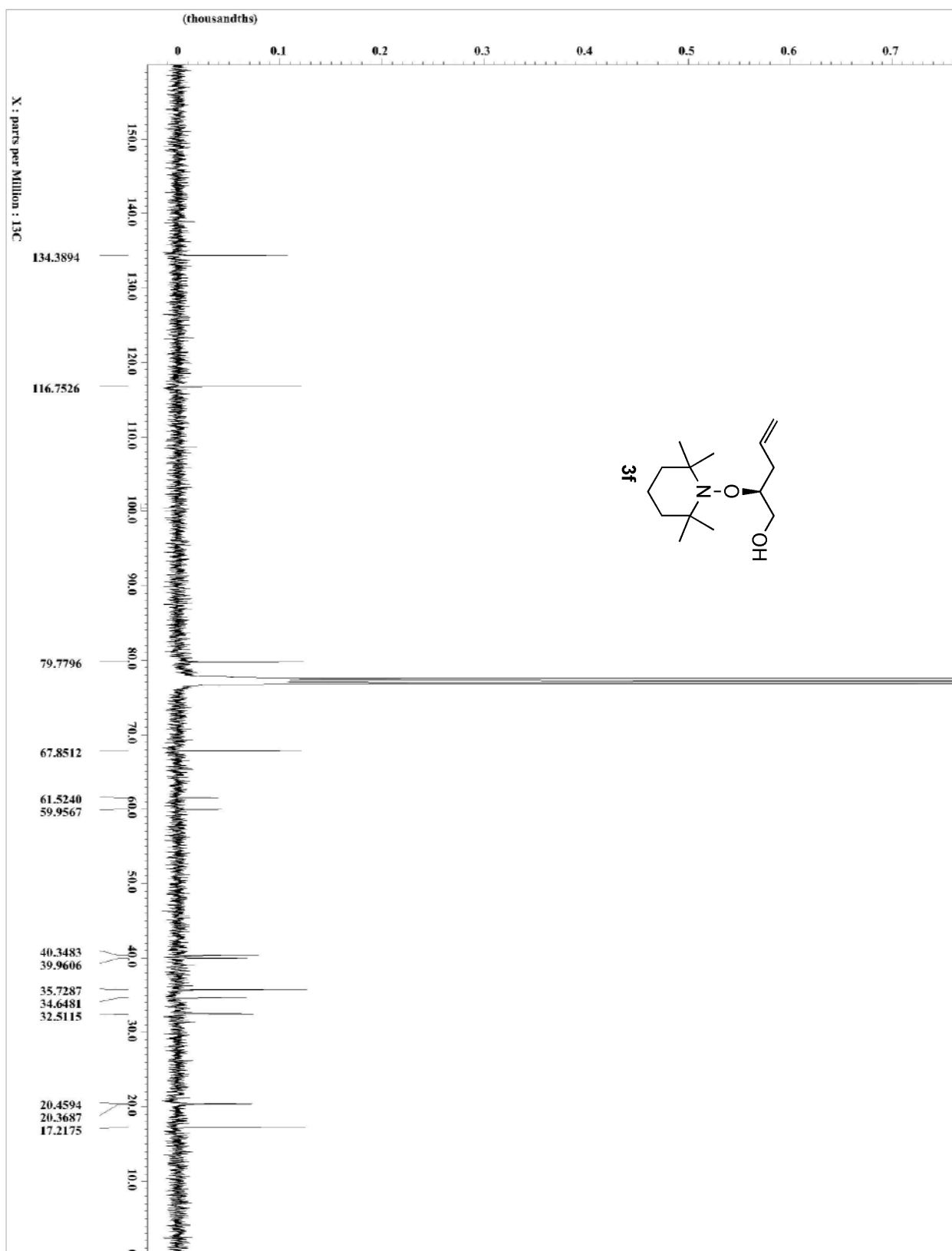


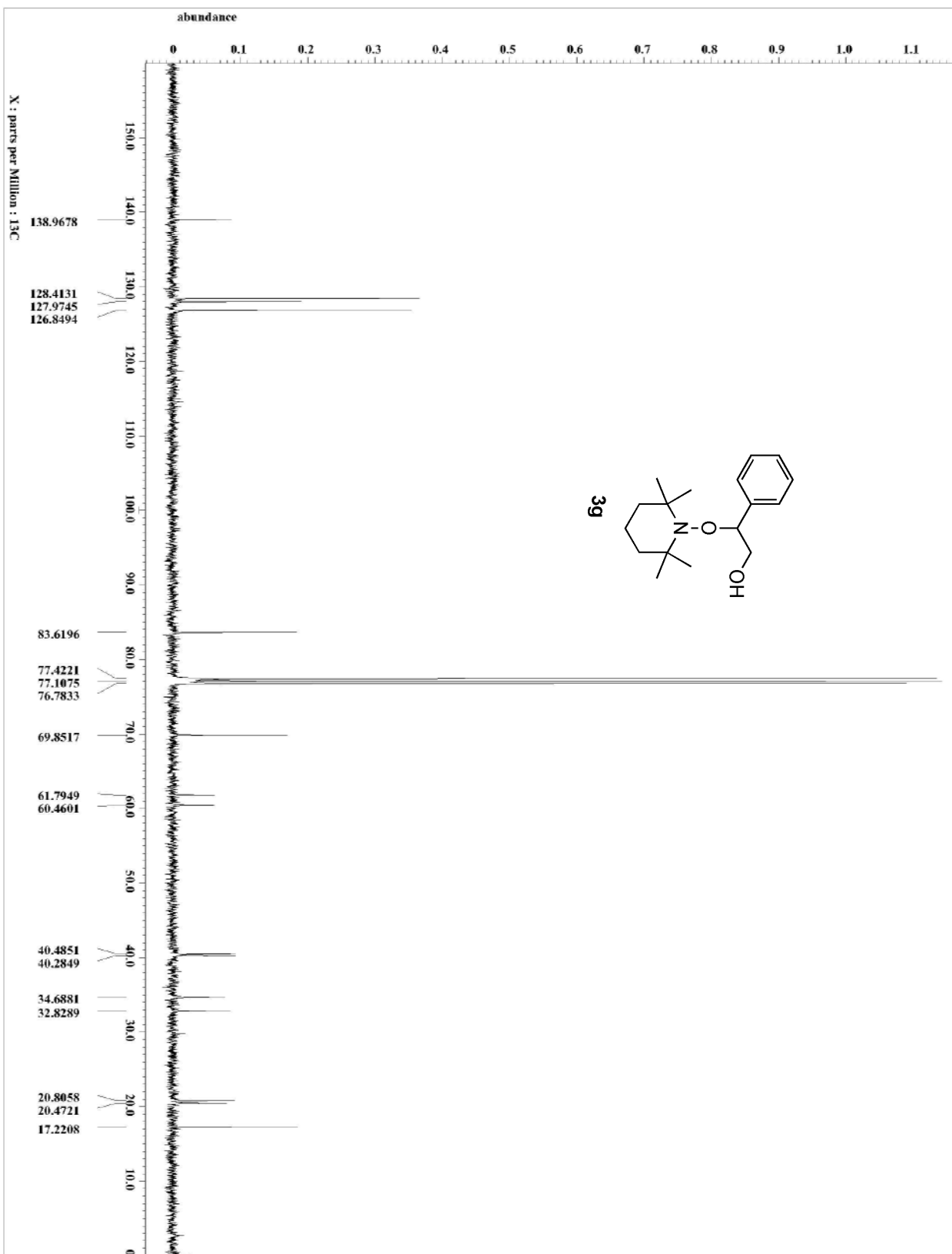






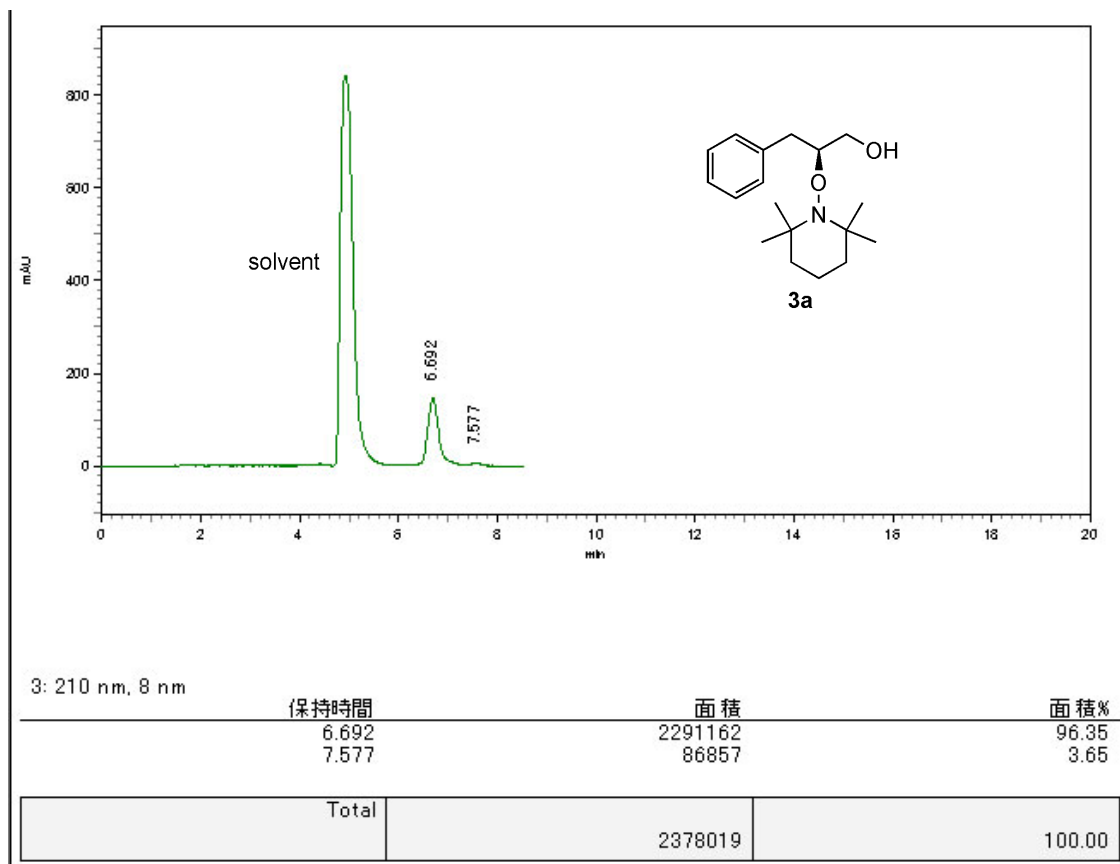




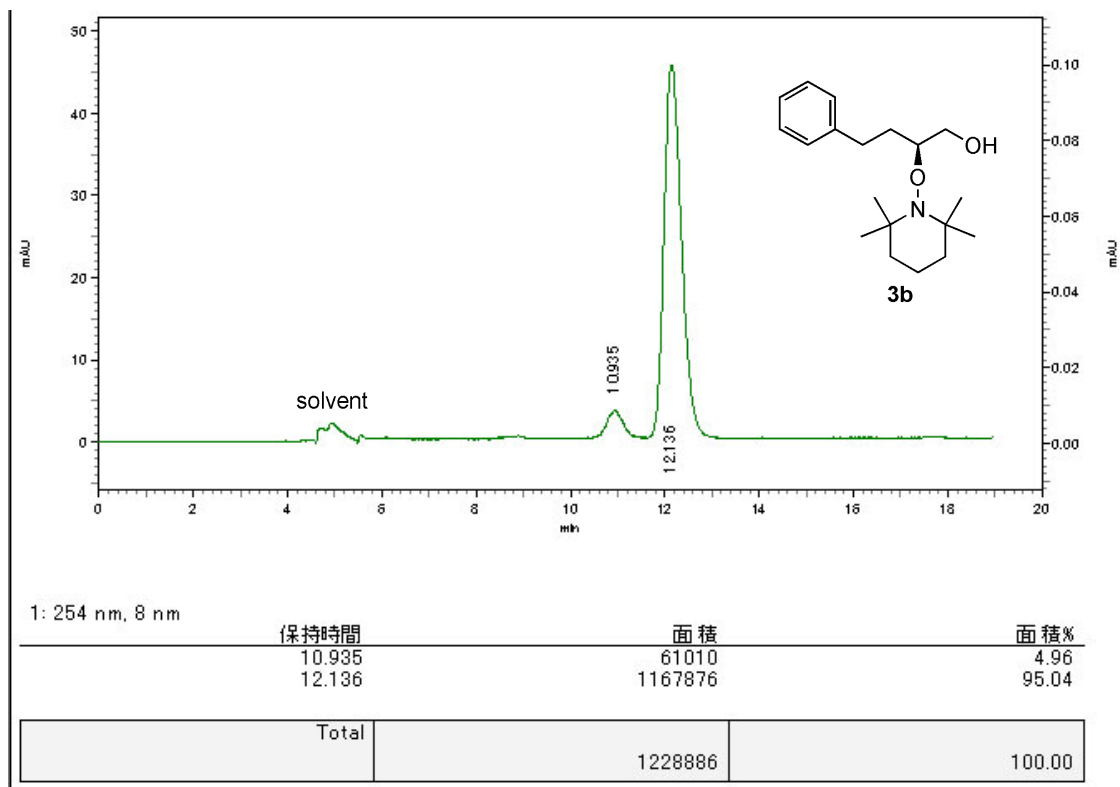


HPLC analyses

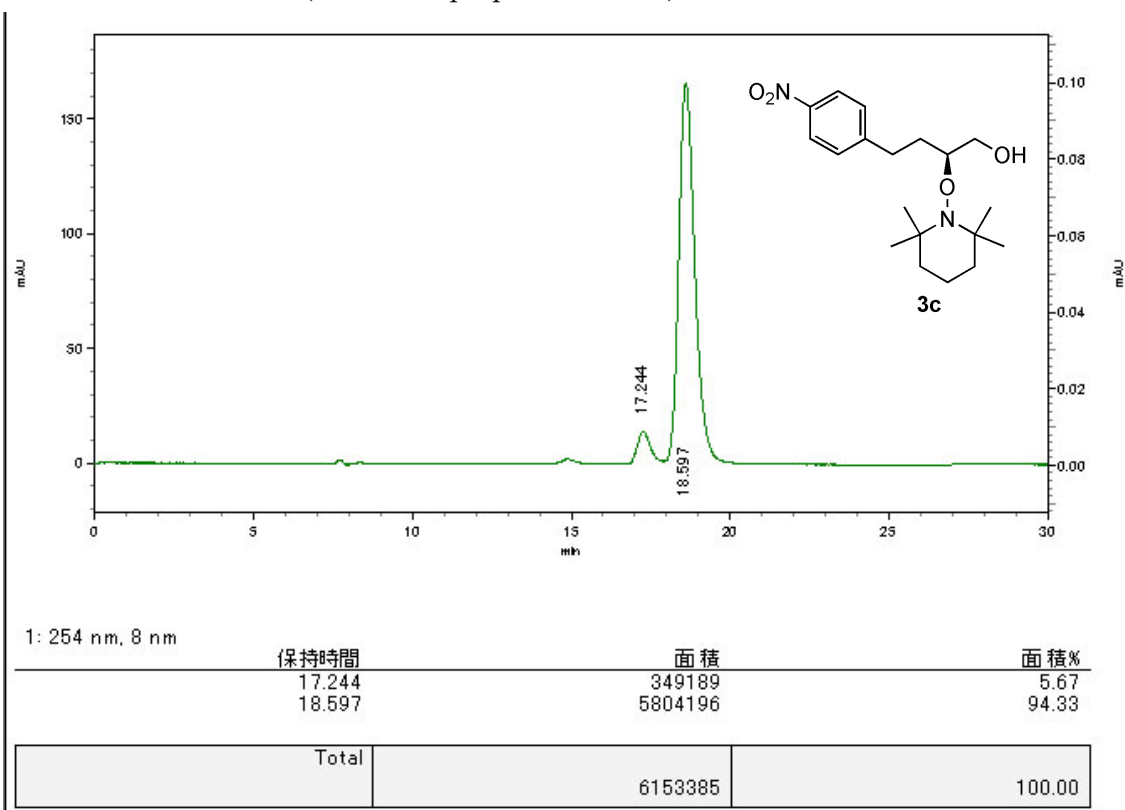
Chiralcel OD-H column, hexane/2-propanol = 98/2, 1.0 mL min⁻¹



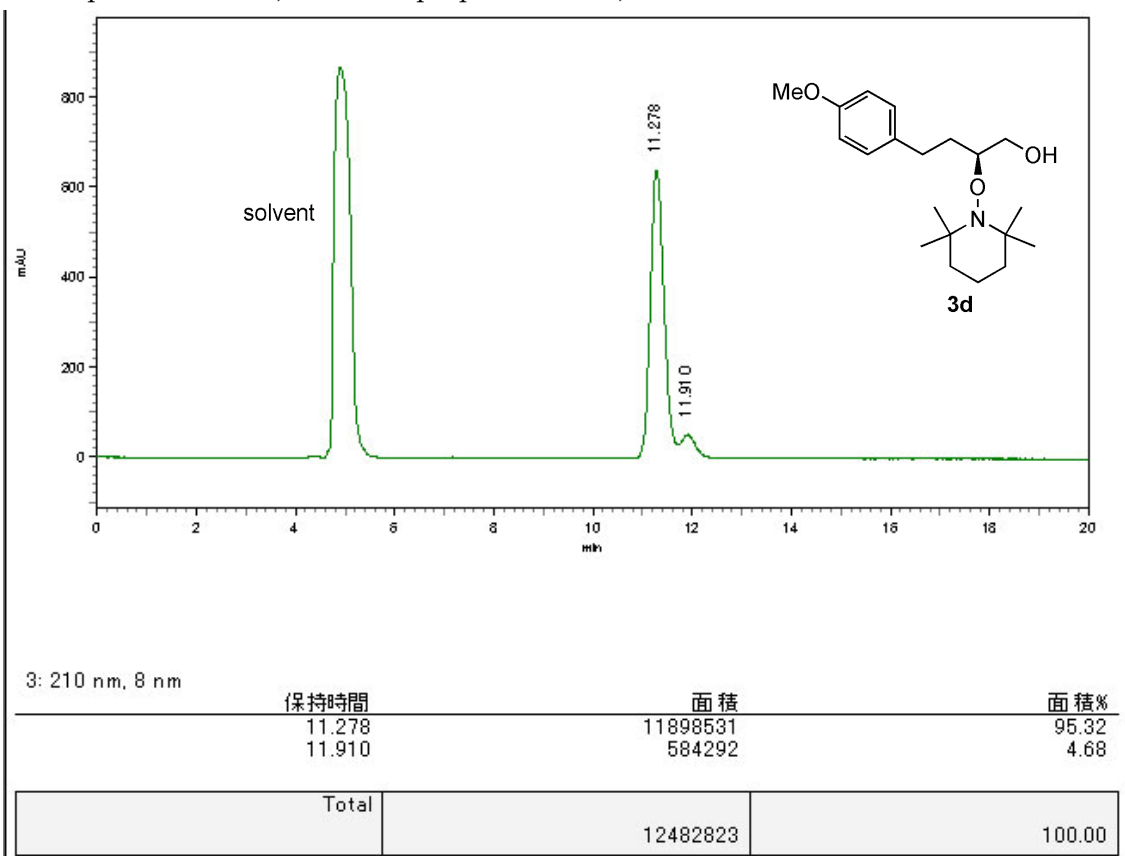
Chiralcel OD-H column, hexane/2-propanol = 98/2, 1.0 mL min⁻¹



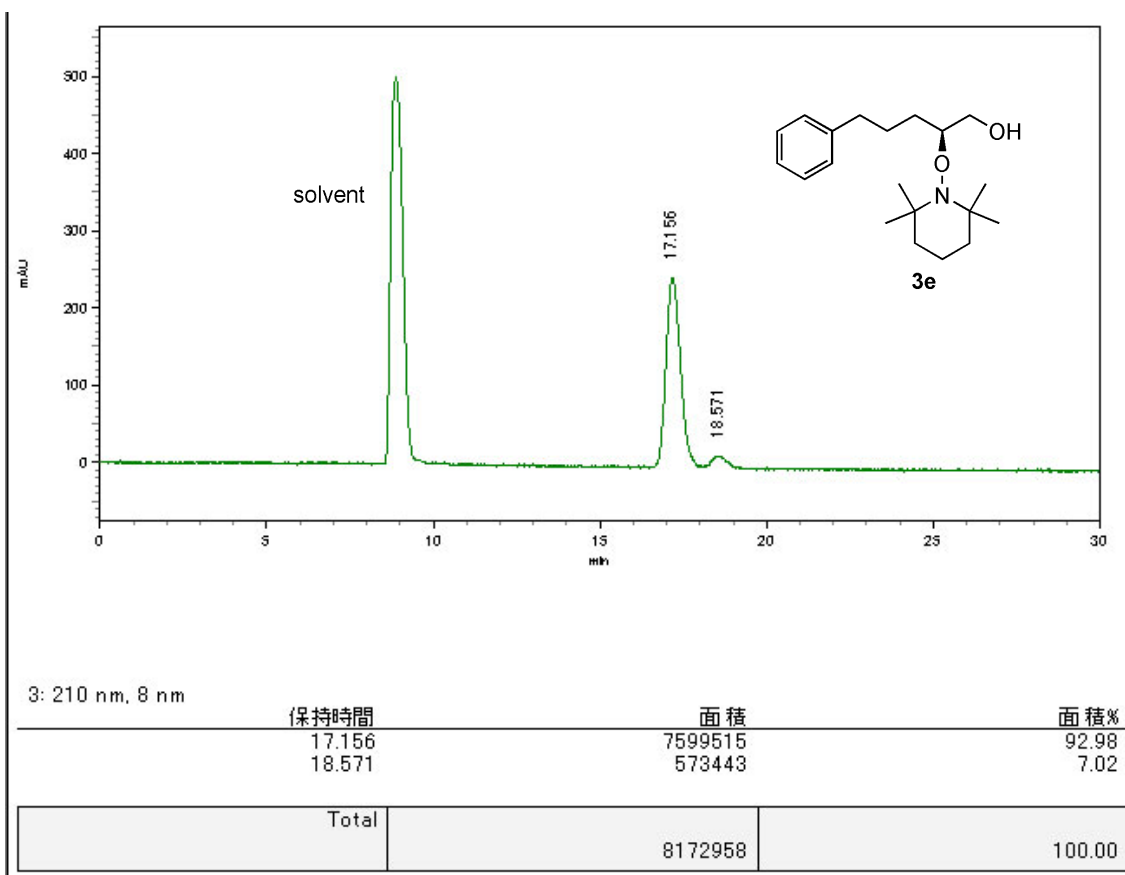
Chiralcel OD-H column, hexane/2-propanol = 90/10, 0.5 mL min⁻¹



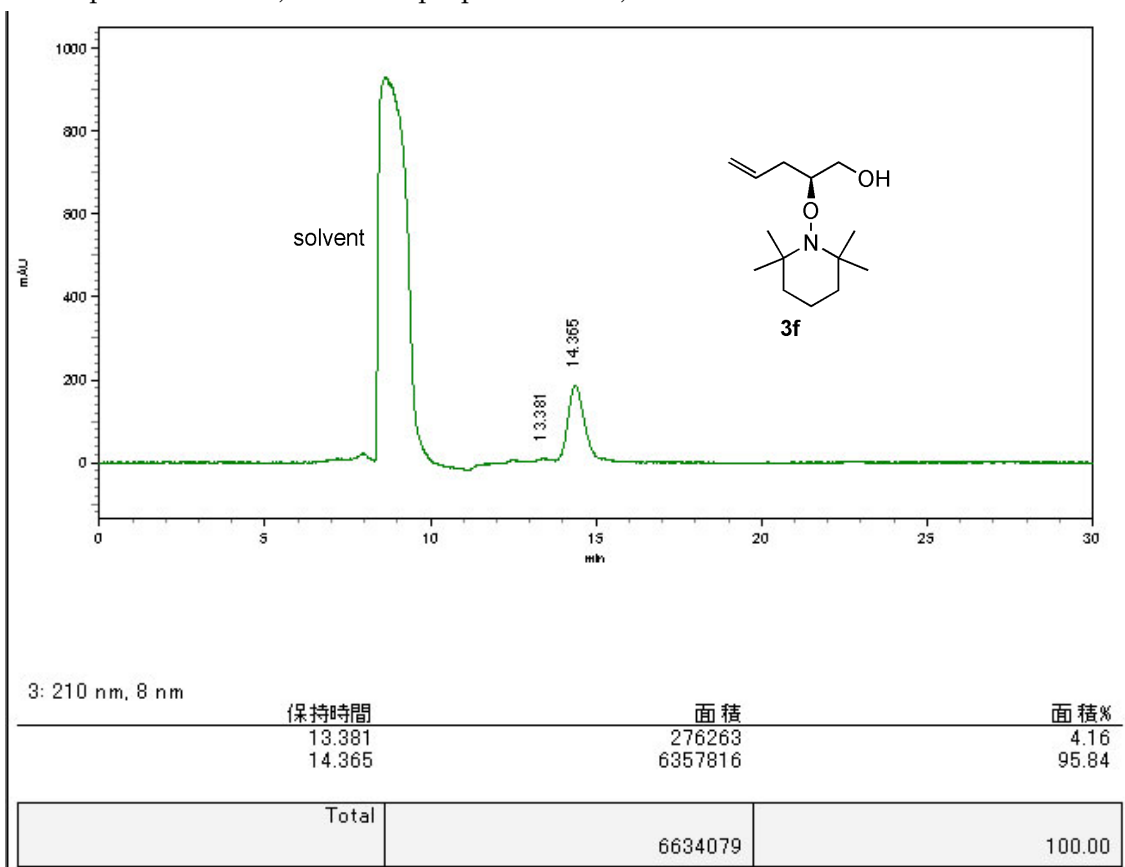
Chiralpak IA column, hexane/2-propanol = 98/2, 1.0 mL min⁻¹



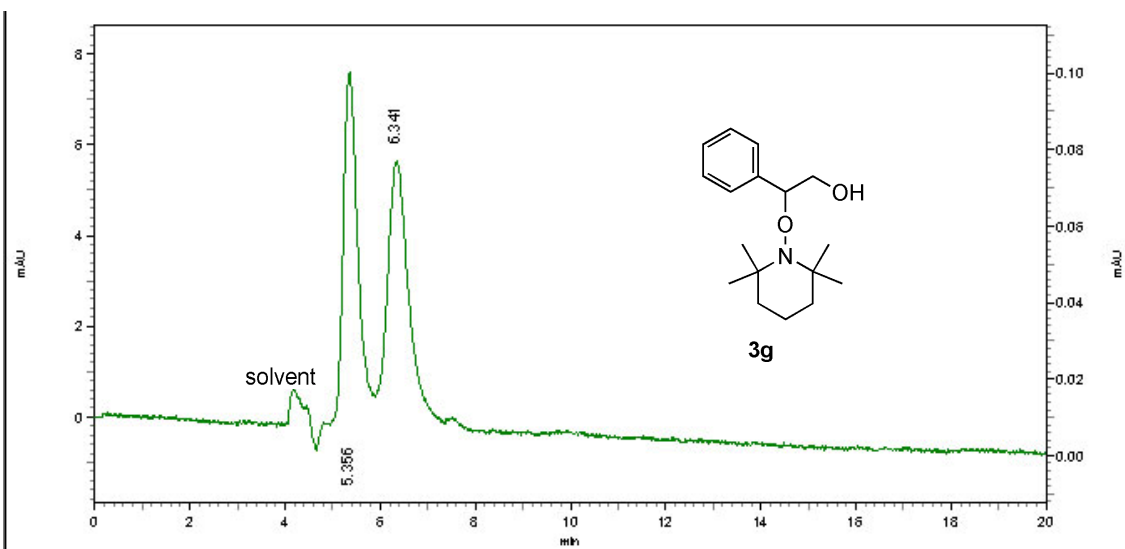
Chiralcel OD-H column, hexane/2-propanol = 98/2, 1.0 mL min⁻¹



Chiralpak IA column, hexane/2-propanol = 99/1, 0.5 mL min⁻¹



Chiralcel OJ column, hexane/2-propanol = 98/2, 1.0 mL min⁻¹



1: 260 nm, 8 nm

保持時間	面積	面積%
5.356	166072	48.07
6.341	179425	51.93
Total	345497	100.00

FAB Mass spectra

(matrix: 3-nitrobenzyl alcohol, positive ionization mode)

